



Clinical trial results:

A Phase 2 Open-Label Single-Arm Study to Evaluate the Efficacy and Safety of Loncastuximab Tesirine in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL) (LOTIS-2)

Summary

EudraCT number	2017-004288-11
Trial protocol	GB IT
Global end of trial date	09 August 2022

Results information

Result version number	v1 (current)
This version publication date	19 August 2023
First version publication date	19 August 2023

Trial information

Trial identification

Sponsor protocol code	ADCT-402-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03589469
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ADC Therapeutics SA
Sponsor organisation address	Route de la Corniche, 3B, Epalinges, Switzerland, 1066
Public contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.com
Scientific contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 September 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of single agent loncastuximab tesirine in participants with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL).

Protection of trial subjects:

This study was conducted in compliance with the Declaration of Helsinki and with Good Clinical Practices.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 31
Country: Number of subjects enrolled	Italy: 53
Country: Number of subjects enrolled	United States: 59
Country: Number of subjects enrolled	Switzerland: 2
Worldwide total number of subjects	145
EEA total number of subjects	53

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	65

From 65 to 84 years	78
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled at 28 study sites in Italy, Switzerland, the United Kingdom, and the United States from 01 August 2018 to 09 August 2022.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Loncastuximab Tesirine
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Arm description:

Participants received loncastuximab tesirine as an intravenous (IV) infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once every 3 weeks (Q3W) for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Loncastuximab tesirine
Investigational medicinal product code	ADCT-402
Other name	Zynlonta
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

intravenous infusion

Number of subjects in period 1	Loncastuximab Tesirine
Started	145
Completed	11
Not completed	134
Physician decision	20
Consent withdrawn by subject	8
Death	97
Miscellaneous	1
Lost to follow-up	8

Baseline characteristics

Reporting groups

Reporting group title	Loncastuximab Tesirine
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Reporting group description:

Participants received loncastuximab tesirine as an intravenous (IV) infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once every 3 weeks (Q3W) for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first.

Reporting group values	Loncastuximab Tesirine	Total	
Number of subjects	145	145	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	62.7		
standard deviation	± 13.63	-	
Gender categorical			
Units: Subjects			
Female	60	60	
Male	85	85	
Ethnicity			
Units: Subjects			
Hispanic or Latino	13	13	
Not Hispanic or Latino	132	132	
Unknown or Not Reported	0	0	
Race			
Units: Subjects			
White	130	130	
Black or African American	5	5	
Asian	3	3	
American Indian or Alaskan Native	1	1	
Native Hawaiian or Pacific Islander	1	1	
Other	5	5	

End points

End points reporting groups

Reporting group title	Loncastuximab Tesirine
Reporting group description: Participants received loncastuximab tesirine as an intravenous (IV) infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once every 3 weeks (Q3W) for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first.	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR) ^[1]
End point description: ORR, as determined by central review according to the 2014 Lugano classification, defined as the percentage of participants with a best overall response (BOR) of complete response (CR) or partial response (PR). All-treated population - all participants who received at least 1 dose of treatment.	
End point type	Primary
End point timeframe: Up to 21.5 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No additional statistical analyses were pre-specified for this endpoint.

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: percentage of participants				
number (confidence interval 95%)	48.3 (39.9 to 56.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
End point description: DOR defined as the time from the first documentation of tumor response to disease progression or death. Participants in the all-treated population who achieved a CR or PR. Values of "99999" indicate the upper confidence interval could not be calculated due to insufficient number of participants with events.	
End point type	Secondary
End point timeframe: Up to 39 months	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: months				
median (confidence interval 95%)	13.37 (6.87 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-free Survival (RFS)

End point title	Relapse-free Survival (RFS)
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End point description:

RFS was defined as the time from the documentation of CR to disease progression or death. Participants in the all-treated population who achieved CR.

Values of "99999" indicate the median, lower and upper confidence interval could not be calculated due to insufficient number of participants with events.

End point type	Secondary
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End point timeframe:

Up to 39 months

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response (CR) Rate

End point title	Complete Response (CR) Rate
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End point description:

CR rate defined as the percentage of treated participants with a BOR of CR. All-treated population - all participants who received at least 1 dose of treatment.

End point type	Secondary
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End point timeframe:

Up to 39 months

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: percentage of participants				
number (confidence interval 95%)	24.8 (18.0 to 32.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
End point description: PFS was defined as the time between start of treatment and the first documentation of recurrence, progression, or death. All-treated population - all participants who received at least 1 dose of treatment.	
End point type	Secondary
End point timeframe: Up to 40 months	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: months				
median (confidence interval 95%)	4.93 (2.89 to 8.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experience Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants Who Experience Treatment-emergent Adverse Events (TEAEs)
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End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product that did not necessarily have to have a causal relationship with treatment. A TEAE was an adverse event with an onset that began or worsened

on or after the first dose date and until 30 days after the last dose date, or start of a new anticancer therapy/procedure, whichever came earlier. TEAE assessments also included those per the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 Grade ≥ 3 AEs and serious TEAEs.

AEs were graded using CTCAE version 4 and according to the following: Grade 1 = mild AE, Grade 2 = Moderate AE, Grade 3 = a severe AE, Grade 4 = life-threatening AE, and Grade 5 = death due to AE. For events not listed in the CTCAE criteria, the same grading was used. All-treated population - all participants who received at least 1 dose of treatment.

End point type	Secondary
End point timeframe:	
Up to 599 days	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: participants				
Any TEAE	143			
Grade ≥ 3 TEAE	107			
Serious TEAE	57			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time between the start of treatment and death from any cause. All-treated population - all participants who received at least 1 dose of treatment.	
End point type	Secondary
End point timeframe:	
Up to 43 months	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: months				
median (confidence interval 95%)	9.53 (6.74 to 11.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Change From Baseline in Vital Signs

End point title	Number of Participants With Clinically Significant Change From Baseline in Vital Signs
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End point description:

Vital sign measurements included arterial blood pressure, heart rate, respiratory rate, and body temperature. Clinical significance was determined by the investigator. All-treated population - all participants who received at least 1 dose of treatment.

End point type	Secondary
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End point timeframe:

Baseline up to 599 days

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes From Baseline in Clinical Laboratory Tests

End point title	Number of Participants With Clinically Significant Changes From Baseline in Clinical Laboratory Tests
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End point description:

Clinical laboratory tests included hematology and chemistry. Clinically significant changes were determined by the Investigator. All-treated population - all participants who received at least 1 dose of treatment.

End point type	Secondary
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End point timeframe:

Baseline up to 599 days

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: participants	83			

Statistical analyses

No statistical analyses for this end point

Secondary: Eastern Cooperative Oncology Group (ECOG) Performance Status at Baseline and End of Treatment

End point title	Eastern Cooperative Oncology Group (ECOG) Performance Status at Baseline and End of Treatment
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End point description:

ECOG (Eastern Cooperative Oncology Group) Performance Status is scored on a 6-point scale where higher scores indicate a worse outcome. ECOG scores include the following:

- 0 = fully active, able to carry on all pre-disease performance without restriction
- 1 = restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
- 2 = ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours
- 3 = capable of only limited self-care; confined to bed or chair more than 50% of waking hours
- 4 = completely disabled; cannot carry on any self-care; totally confined to bed or chair
- 5 = dead.

All-treated population - all participants who received at least 1 dose of treatment. Results are presented for participants with data available for analysis at end of treatment.

End point type	Secondary
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End point timeframe:

Baseline and end of treatment (up to 599 days)

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145 ^[2]			
Units: participants				
Baseline: ECOG score 0	58			
Baseline: ECOG score 1	78			
Baseline: ECOG score 2	9			
Baseline: ECOG score 3	0			
Baseline: ECOG score 4	0			
Baseline: ECOG score 5	0			
End of treatment: ECOG score 0	44			
End of treatment: ECOG score 1	50			
End of treatment: ECOG score 2	14			
End of treatment: ECOG score 3	2			
End of treatment: ECOG score 4	1			
End of treatment: ECOG score 5	0			

Notes:

[2] - Baseline n = 145; End of treatment n = 111.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Change From Baseline in 12-lead Electrocardiograms (ECGs)

End point title	Number of Participants With Clinically Significant Change From Baseline in 12-lead Electrocardiograms (ECGs)
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End point description:

Clinically significant changes from baseline for 12-lead ECGs were measured as abnormal QT interval corrected by Fridericia formula (QTcF) and QT interval corrected by Bazett formula (QTcB) values. All-treated population - all participants who received at least 1 dose of treatment.

End point type	Secondary
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End point timeframe:

Baseline up to 599 days

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: participants				
QTcB maximum change from baseline: >30, ≤60 msec	30			
QTcB maximum change from baseline: >60 msec	4			
QTcF maximum change from baseline: >30, ≤60 msec	23			
QTcF maximum change from baseline: >60 msec	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Concentration (Cmax) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

End point title	Maximum Concentration (Cmax) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199
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End point description:

Pharmacokinetic (PK) population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

End point type	Secondary
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End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose and end of infusion.

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	142			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Conjugated Antibody Cycle 1 (n = 142)	2430 (± 38.8)			
Conjugated Antibody Cycle 2 (n = 117)	2734 (± 35.8)			

Conjugated Antibody Cycle 3 (n = 83)	1694 (± 47.6)			
Total Antibody Cycle 1 (n = 142)	3267 (± 36.7)			
Total Antibody Cycle 2 (n = 117)	3756 (± 31.3)			
Total Antibody Cycle 3 (n = 81)	2581 (± 41.9)			
SG3199 Cycle 1 (n = 8)	0.0410 (± 56.6)			
SG3199 Cycle 2 (n = 5)	0.0490 (± 78.8)			
SG3199 Cycle 3 (n = 3)	0.0320 (± 20.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUC0-last) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

End point title	Area Under the Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUC0-last) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199
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End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

End point type	Secondary
End point timeframe:	Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	143			
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Conjugated Antibody Cycle 1 (n = 143)	15850 (± 105)			
Conjugated Antibody Cycle 2 (n = 116)	23913 (± 67.1)			
Conjugated Antibody Cycle 3 (n = 0)	99999 (± 99999)			
Total Antibody Cycle 1 (n = 143)	22160 (± 106)			
Total Antibody Cycle 2 (n = 116)	33762 (± 67.2)			
Total Antibody Cycle 3 (n = 0)	99999 (± 99999)			
SG3199 Cycle 1 (n = 8)	0.00400 (± 576)			
SG3199 Cycle 2 (n = 5)	0.00100 (± 204)			

SG3199 Cycle 3 (n = 0)	99999 (± 99999)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Curve From Time Zero to Infinity (AUC_{0-∞}) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

End point title	Area Under the Concentration-time Curve From Time Zero to Infinity (AUC _{0-∞}) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199
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End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

End point type	Secondary
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End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Conjugated Antibody Cycle 1 (n = 32)	19825 (± 52.9)			
Conjugated Antibody Cycle 2 (n = 99)	26902 (± 33.4)			
Conjugated Antibody Cycle 3 (n = 0)	99999 (± 99999)			
Total Antibody Cycle 1 (n = 27)	25778 (± 61.3)			
Total Antibody Cycle 2 (n = 97)	37761 (± 30.4)			
Total Antibody Cycle 3 (n = 0)	99999 (± 99999)			
SG3199 Cycle 1 (n = 0)	99999 (± 99999)			
SG3199 Cycle 2 (n = 0)	99999 (± 99999)			
SG3199 Cycle 3 (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Terminal Half-life (Thalf) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

End point title	Apparent Terminal Half-life (Thalf) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199
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End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

End point type	Secondary
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End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: days				
geometric mean (geometric coefficient of variation)				
Conjugated Antibody Cycle 1 (n = 32)	8.85 (± 53.5)			
Conjugated Antibody Cycle 2 (n = 90)	15.2 (± 31.7)			
Conjugated Antibody Cycle 3 (n = 0)	99999 (± 99999)			
Total Antibody Cycle 1 (n = 27)	8.66 (± 54.6)			
Total Antibody Cycle 2 (n = 63)	20.9 (± 56.5)			
Total Antibody Cycle 3 (n = 0)	99999 (± 99999)			
SG3199 Cycle 1 (n = 0)	99999 (± 99999)			
SG3199 Cycle 2 (n = 0)	99999 (± 99999)			
SG3199 Cycle 3 (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

End point title	Apparent Clearance (CL) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199
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End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

End point type	Secondary
End point timeframe:	
Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: L/day				
geometric mean (geometric coefficient of variation)				
Conjugated Antibody Cycle 1 (n = 32)	0.458 (± 47.6)			
Conjugated Antibody Cycle 2 (n = 99)	0.331 (± 32.0)			
Total Antibody Cycle 1 (n = 27)	0.418 (± 56.5)			
Total Antibody Cycle 2 (n = 97)	0.285 (± 31.3)			
SG3199 Cycle 1 (n = 0)	99999 (± 99999)			
SG3199 Cycle 2 (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution at Steady State (Vss) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

End point title	Apparent Volume of Distribution at Steady State (Vss) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199
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End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

End point type	Secondary
End point timeframe:	
Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: liters				
geometric mean (geometric coefficient of variation)				

Conjugated Antibody Cycle 1 (n = 32)	4.24 (± 39.6)			
Conjugated Antibody Cycle 2 (n = 90)	6.40 (± 36.5)			
Conjugated Antibody Cycle 3 (n = 0)	99999 (± 99999)			
Total Antibody Cycle 1 (n = 27)	4.10 (± 36.4)			
Total Antibody Cycle 2 (n = 63)	7.54 (± 58.9)			
Total Antibody Cycle 3 (n = 0)	99999 (± 99999)			
SG3199 Cycle 1 (n = 0)	99999 (± 99999)			
SG3199 Cycle 2 (n = 0)	99999 (± 99999)			
SG3199 Cycle 3 (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Index (AI) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

End point title	Accumulation Index (AI) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199
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End point description:

AI is the ratio of AUC_{0-last} for each cycle divided by AUC_{0-last} of the previous cycle. PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre- Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

End point type	Secondary
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End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: ratio				
geometric mean (geometric coefficient of variation)				
Conjugated Antibody Cycle 1 (n = 0)	99999 (± 99999)			
Conjugated Antibody Cycle 2 (n = 90)	1.65 (± 18.5)			
Conjugated Antibody Cycle 3 (n = 0)	99999 (± 99999)			
Total Antibody Cycle 1 (n = 0)	99999 (± 99999)			
Total Antibody Cycle 2 (n = 63)	2.07 (± 38.1)			
Total Antibody Cycle 3 (n = 0)	99999 (± 99999)			

SG3199 Cycle 1 (n = 0)	99999 (± 99999)			
SG3199 Cycle 2 (n = 0)	99999 (± 99999)			
SG3199 Cycle 3 (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With an Anti-drug Antibody (ADA) Response to Loncastuximab Tesirine

End point title	Number of Participants With an Anti-drug Antibody (ADA) Response to Loncastuximab Tesirine
End point description:	All-treated population - all participants who received at least 1 dose of treatment.
End point type	Secondary
End point timeframe:	Up to 599 days

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: participants				
Confirmed Positive ADA Pre-dose	1			
Confirmed Positive ADA Post-dose Only	0			
Confirmed Positive ADA Anytime	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Score in the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) Visual Analogue Scale (VAS)

End point title	Change From Baseline Score in the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) Visual Analogue Scale (VAS)
End point description:	EQ-5D-5L is designed as an international, standardized, instrument for describing and evaluating quality of life (QoL). In the EQ-5D-5L VAS participants are asked to indicate their health state today on a VAS with the endpoints labeled 'the best health you can imagine' (score 100) and 'the worst health you can imagine' (score 0). A higher score on the VAS indicates better health related QoL. A positive change from baseline indicates an improvement in health related QoL. Patient reported outcome (PRO) population. Only participants with data available for analysis are included. Number of subjects analysed represents all participants who contributed data to this assessment, though not all participants contributed data to each time point.

Values of "99999" indicate standard deviation could not be calculated as n = 1.

End point type	Secondary
End point timeframe:	
Baseline, Day 1 of Cycles 2 to 26 (cycle duration of 3 weeks), and end of treatment (up to 599 days)	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	130			
Units: score on a scale				
arithmetic mean (standard deviation)				
Cycle 2 Day 1 (n = 108)	-0.1 (± 15.97)			
Cycle 3 Day 1 (n = 76)	1.3 (± 16.85)			
Cycle 4 Day 1 (n = 58)	2.8 (± 15.00)			
Cycle 5 Day 1 (n = 44)	2.8 (± 13.50)			
Cycle 6 Day 1 (n = 33)	3.0 (± 17.45)			
Cycle 7 Day 1 (n = 28)	4.0 (± 12.91)			
Cycle 8 Day 1 (n = 22)	7.3 (± 12.87)			
Cycle 9 Day 1 (n = 20)	7.7 (± 15.69)			
Cycle 10 Day 1 (n = 13)	12.2 (± 15.64)			
Cycle 11 Day 1 (n = 12)	11.8 (± 17.62)			
Cycle 12 Day 1 (n = 10)	16.3 (± 16.06)			
Cycle 13 Day 1 (n = 8)	6.0 (± 16.54)			
Cycle 14 Day 1 (n = 6)	12.2 (± 15.43)			
Cycle 15 Day 1 (n = 5)	6.6 (± 12.36)			
Cycle 16 Day 1 (n = 4)	5.5 (± 13.70)			
Cycle 17 Day 1 (n = 4)	8.3 (± 13.62)			
Cycle 18 Day 1 (n = 3)	11.0 (± 11.53)			
Cycle 19 Day 1 (n = 2)	11.5 (± 16.26)			
Cycle 20 Day 1 (n = 1)	23.0 (± 99999)			
Cycle 21 Day 1 (n = 2)	16.5 (± 9.19)			
Cycle 22 Day 1 (n = 2)	16.5 (± 9.19)			
Cycle 23 Day 1 (n = 1)	23.0 (± 99999)			
Cycle 24 Day 1 (n = 1)	23.0 (± 99999)			
Cycle 25 Day 1 (n = 1)	23.0 (± 99999)			
Cycle 26 Day 1 (n = 1)	23.0 (± 99999)			
End of treatment (n = 98)	-8.3 (± 19.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Score in the Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) - Lymphoma Subscale (LymS)

End point title	Change From Baseline Score in the Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) - Lymphoma Subscale (LymS)
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End point description:

Composed of the Functional Assessment of Cancer Therapy - General (FACT-G) plus the 15-item LymS. The FACTG questionnaire contains 27 items covering 4 core health related quality of life (QoL) subscales: Physical Wellbeing (7 items), Social/Family Wellbeing (7), Emotional Wellbeing (6), and Functional Wellbeing (7). The LymS addresses issues including pain, itching, night sweats, trouble sleeping, fatigue and trouble concentrating. Score range for the LymS was 0 - 60, where a higher score indicates less symptoms. The LymS score is reported. A positive change from baseline indicates an improvement in health related QoL. PRO population. Only participants with data available for analysis are included. Number of subjects analysed represents all participants who contributed data to this assessment, though not all participants contributed data to each time point.

Values of "9999" indicate n = 0; "99999" indicate standard deviation could not be calculated as n = 1.

End point type	Secondary
End point timeframe:	
Baseline, Day 1 of Cycles 2 to 25 (cycle duration of 3 weeks), and end of treatment (up to 599 days)	

End point values	Loncastuximab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	130			
Units: score on a scale				
arithmetic mean (standard deviation)				
Cycle 2 Day 1 (n = 110)	0.95 (± 7.114)			
Cycle 3 Day 1 (n = 78)	1.34 (± 8.764)			
Cycle 4 Day 1 (n = 60)	2.09 (± 8.832)			
Cycle 5 Day 1 (n = 47)	0.16 (± 8.506)			
Cycle 6 Day 1 (n = 33)	1.16 (± 9.918)			
Cycle 7 Day 1 (n = 29)	1.00 (± 11.474)			
Cycle 8 Day 1 (n = 22)	3.43 (± 10.141)			
Cycle 9 Day 1 (n = 20)	2.17 (± 9.498)			
Cycle 10 Day 1 (n = 13)	3.18 (± 11.769)			
Cycle 11 Day 1 (n = 12)	4.35 (± 13.053)			
Cycle 12 Day 1 (n = 10)	4.90 (± 11.140)			
Cycle 13 Day 1 (n = 9)	2.01 (± 16.871)			
Cycle 14 Day 1 (n = 6)	0.63 (± 17.442)			
Cycle 15 Day 1 (n = 5)	-3.27 (± 7.691)			
Cycle 16 Day 1 (n = 4)	-8.04 (± 10.561)			
Cycle 17 Day 1 (n = 4)	-6.88 (± 9.360)			
Cycle 18 Day 1 (n = 3)	-5.00 (± 7.937)			
Cycle 19 Day 1 (n = 2)	-1.00 (± 4.243)			
Cycle 20 Day 1 (n = 2)	-2.25 (± 4.596)			
Cycle 21 Day 1 (n = 2)	-0.50 (± 2.121)			

Cycle 22 Day 1 (n = 2)	-1.00 (± 2.828)			
Cycle 23 Day 1 (n = 1)	1.00 (± 99999)			
Cycle 24 Day 1 (n = 0)	9999 (± 9999)			
Cycle 25 Day 1 (n = 1)	1.00 (± 99999)			
End of treatment (n = 98)	-1.19 (± 9.042)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 43 months

Adverse event reporting additional description:

All non-serious AEs at a frequency threshold of $\geq 5\%$ and all SAEs, regardless of relationship to study drug, were collected from the time the participant signs the ICF until 30 days after the last dose of study drug or start of new anti-cancer therapy, whichever is earlier; thereafter, only related SAEs were collected, with two exceptions.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Loncastuximab Tesirine
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Reporting group description:

Participants received loncastuximab tesirine as an IV infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once Q3W for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first.

Serious adverse events	Loncastuximab Tesirine		
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 145 (39.31%)		
number of deaths (all causes)	97		
number of deaths resulting from adverse events	8		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
alternative assessment type:			

Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Embolism				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Disease progression				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Fatigue				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Face oedema				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
alternative assessment type: Systematic				

subjects affected / exposed	4 / 145 (2.76%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleuritic pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 145 (2.07%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intentional self-injury			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericarditis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Psychomotor skills impaired			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Facial nerve disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 145 (3.45%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestinal obstruction			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 145 (2.07%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Small intestinal perforation				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			

Renal and urinary disorders			
Acute kidney injury			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Hydronephrosis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Neck pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Rhinovirus infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia fungal			

alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 145 (1.38%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Metapneumovirus infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection bacterial			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 145 (4.14%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Dehydration			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Loncastuximab Tesarine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 145 (95.86%)		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	29 / 145 (20.00%)		
occurrences (all)	35		
Aspartate aminotransferase increased			
subjects affected / exposed	23 / 145 (15.86%)		
occurrences (all)	36		
Alanine aminotransferase increased			
subjects affected / exposed	22 / 145 (15.17%)		
occurrences (all)	27		
Weight increased			
subjects affected / exposed	10 / 145 (6.90%)		
occurrences (all)	11		
Gamma-glutamyltransferase increased			
subjects affected / exposed	61 / 145 (42.07%)		
occurrences (all)	74		
Vascular disorders			
Hypotension			
subjects affected / exposed	10 / 145 (6.90%)		
occurrences (all)	12		
Hypertension			
subjects affected / exposed	8 / 145 (5.52%)		
occurrences (all)	12		
Cardiac disorders			
Tachycardia			

subjects affected / exposed occurrences (all)	11 / 145 (7.59%) 12		
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 145 (6.21%)		
occurrences (all)	9		
Headache			
subjects affected / exposed	15 / 145 (10.34%)		
occurrences (all)	20		
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	11 / 145 (7.59%)		
occurrences (all)	18		
Leukopenia			
subjects affected / exposed	21 / 145 (14.48%)		
occurrences (all)	34		
Anaemia			
subjects affected / exposed	38 / 145 (26.21%)		
occurrences (all)	54		
Thrombocytopenia			
subjects affected / exposed	48 / 145 (33.10%)		
occurrences (all)	73		
Neutropenia			
subjects affected / exposed	58 / 145 (40.00%)		
occurrences (all)	100		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	14 / 145 (9.66%)		
occurrences (all)	16		
Pyrexia			
subjects affected / exposed	25 / 145 (17.24%)		
occurrences (all)	38		
Oedema peripheral			
subjects affected / exposed	28 / 145 (19.31%)		
occurrences (all)	33		
Fatigue			

subjects affected / exposed	40 / 145 (27.59%)		
occurrences (all)	44		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	25 / 145 (17.24%)		
occurrences (all)	34		
Nausea			
subjects affected / exposed	34 / 145 (23.45%)		
occurrences (all)	42		
Abdominal pain			
subjects affected / exposed	16 / 145 (11.03%)		
occurrences (all)	18		
Constipation			
subjects affected / exposed	17 / 145 (11.72%)		
occurrences (all)	17		
Vomiting			
subjects affected / exposed	19 / 145 (13.10%)		
occurrences (all)	22		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	14 / 145 (9.66%)		
occurrences (all)	15		
Dyspnoea			
subjects affected / exposed	17 / 145 (11.72%)		
occurrences (all)	17		
Cough			
subjects affected / exposed	32 / 145 (22.07%)		
occurrences (all)	33		
Nasal congestion			
subjects affected / exposed	8 / 145 (5.52%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	8 / 145 (5.52%)		
occurrences (all)	8		
Photosensitivity reaction			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Erythema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>15 / 145 (10.34%)</p> <p>18</p> <p>15 / 145 (10.34%)</p> <p>27</p> <p>19 / 145 (13.10%)</p> <p>20</p> <p>19 / 145 (13.10%)</p> <p>20</p>		
<p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>16 / 145 (11.03%)</p> <p>16</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Neck pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>8 / 145 (5.52%)</p> <p>8</p> <p>9 / 145 (6.21%)</p> <p>9</p> <p>9 / 145 (6.21%)</p> <p>9</p>		
<p>Metabolism and nutrition disorders</p> <p>Hypokalaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypophosphataemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Decreased appetite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypomagnesaemia</p>	<p>23 / 145 (15.86%)</p> <p>30</p> <p>23 / 145 (15.86%)</p> <p>33</p> <p>22 / 145 (15.17%)</p> <p>22</p>		

subjects affected / exposed	20 / 145 (13.79%)		
occurrences (all)	23		
Hypocalcaemia			
subjects affected / exposed	12 / 145 (8.28%)		
occurrences (all)	16		
Hyperglycaemia			
subjects affected / exposed	11 / 145 (7.59%)		
occurrences (all)	14		
Hyponatraemia			
subjects affected / exposed	9 / 145 (6.21%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 April 2018	<p>The original protocol was finalized on 09 Mar 2018 and was amended before implementation in response to United States Food and Drug Administration recommendations.</p> <p>The purposes of the amendment were the following:</p> <ul style="list-style-type: none">- The study design was changed to a single cohort with the primary endpoint being ORR in all-treated participants, resulting in changes to primary and secondary objectives and endpoints, and statistical considerations.- For eligibility, pathologic diagnosis was clarified to align with the 2016 World Health Organization classification, the requirement for participants to be ineligible or have failed stem cell transplant (SCT) was removed (as the Agency felt that loncastuximab tesirine was potentially suitable for third line therapy in participants who were potentially eligible for SCT), and the specific requirement for rituximab therapy was deleted as it was expected that all participants would have received this in at least 1 prior line of therapy.- For participants whose disease was not positron-emission tomography (PET)-avid, bone marrow biopsy was added as part of baseline staging and disease assessment if clinically appropriate to fully align with the 2014 Lugano Classification.- Safety follow-up was extended to 180 days after transplant for participants who had responded to loncastuximab tesirine and gone on to SCT to monitor for possible increased transplant-related toxicity in participants who had been treated with loncastuximab tesirine.
24 September 2018	<p>The purposes of the amendment were the following:</p> <ul style="list-style-type: none">- Participants with bulky disease (defined as at least 1 lymph node ≥ 10 cm in longest diameter) were excluded based on analysis of Phase 1 data showing that these participants had an ORR of 11%. Based on an interim analysis this was the ORR at the time of this analysis.- The inclusion criterion regarding hepatic function was revised to no longer allow participants with alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase $\leq 5 \times$ upper limit of normal if there was liver involvement, to be consistent with the requirement to hold the dose of loncastuximab tesirine for participants with Grade ≥ 2 liver function test abnormalities as specified in Section 9.4.5.1.2.- Participants who were clinically benefiting were allowed to continue treatment beyond 1 year with Sponsor review and approval.- A requirement for dose discontinuation for dose delays > 5 weeks due to toxicity at least possibly related to loncastuximab tesirine was added.- The requirement for IV contrast for PET-computer tomography (CT) was removed and the type and timing of efficacy assessments were clarified.
09 July 2019	<p>The purposes of the amendment were the following:</p> <ul style="list-style-type: none">- The text was updated to include information regarding monitoring for extravasation during or after loncastuximab tesirine infusion because of updated safety information.- Efficacy assessments were updated to allow for capture of response information during the follow-up period for participants who received chimeric antigen receptor T-cell (CAR-T) therapy after loncastuximab tesirine treatment.- AE/serious AE reporting requirements for participants who received CAR-T therapy after loncastuximab tesirine discontinuation were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported